```
L1       1107433 S ESCHERICHIA
L2       1180116 S COLI
L3       1098887 S L1 AND L2
L4          4643 S PUR
L5            98 S PUR GENE
L6            47 S L3 AND L5
L7            18 DUP REM L6 (29 DUPLICATES REMOVED)
L8             1 S L7 AND (ATTENUAT?)
L9           212 S CHATFIELD, S/AU
L10           73 DUP REM L9 (139 DUPLICATES REMOVED)
L11            0 S L10 AND MAKOFF
L12            6 S L10 AND L3

     FILE 'BIOSIS, CABA, EMBASE, CAPLUS, LIFESCI, MEDLINE, SCISEARCH' ENTERED
     AT 18:11:02 ON 20 SEP 2003
L13         3595 S GALE
L14       530877 S ATTENUAT?\
L15       530877 S ATTENUAT?
L16           82 S L13 AND L15
L17           43 DUP REM L16 (39 DUPLICATES REMOVED)
L18        10132 S CYA
L19         1381 S L18 AND L1
L20           51 S L19 AND L15
L21           28 DUP REM L20 (23 DUPLICATES REMOVED)
L22          384 S SURA

=> s l22 and l1
L23          115 L22 AND L1
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(FILE 'HOME' ENTERED AT 17:36:16 ON 20 SEP 2003)

FILE 'BIOSIS, CABA, EMBASE, CAPLUS, LIFESCI, MEDLINE, SCISEARCH' ENTERED AT 17:37:25 ON 20 SEP 2003

L1	1107433	S	ESCHERICHIA
L2	1180116	S	COLI
L3	1098887	S	L1 AND L2
L4	4643	S	PUR
L5	98	S	PUR GENE
L6	47	S	L3 AND L5
L7	18		DUP REM L6 (29 DUPLICATES REMOVED)
L8	1	S	L7 AND (ATTENUAT?)
L9	212	S	CHATFIELD, S/AU
L10	73		DUP REM L9 (139 DUPLICATES REMOVED)
L11	0	S	L10 AND MAKOFF
L12	6	S	L10 AND L3

FILE 'BIOSIS, CABA, EMBASE, CAPLUS, LIFESCI, MEDLINE, SCISEARCH' ENTERED AT 18:11:02 ON 20 SEP 2003

L13	3595	S	GALE
L14	530877	S	ATTENUAT?\
L15	530877	S	ATTENUAT?
L16	82	S	L13 AND L15
L17	43		DUP REM L16 (39 DUPLICATES REMOVED)
L18	10132	S	CYA
L19	1381	S	L18 AND L1
L20	51	S	L19 AND L15
L21	28		DUP REM L20 (23 DUPLICATES REMOVED)
L22	384	S	SURA
L23	115	S	L22 AND L1
L24	6	S	L23 AND L15
L25	4643	S	PUR

L7 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3

AB The **Escherichia coli** pur regulon repressor protein was overproduced in a phage T7 expression system. The overexpressed repairs constituted approximately 35% of the soluble cellular protein. Pur repressor was purified to near homogeneity by two chromatographic steps. Hypoxanthine or guanine was required for binding of purified repressor to purF operator DNA. Apparent dissociation constants of 3.4 nM were determined for binding of holorepressor to purF operator and of 1.7 and 7.1 .mu.M were determined for aporepressor interaction with guanine and hypoxanthine, respectively. A requirement for hypoxanthine or guanine for conversion of aporepressor to holorepressor in vitro supports the earlier report (U. Houlberg and K.F. Jensen, J. Bacteriol. 153:837-845, 1983) that these purine bases are involved in regulation of **pur gene** expression in Salmonella typhimurium and confirms that hypoxanthine and guanine are corepressors.

AN 1990:516984 BIOSIS
DN BA90:134260
TI PURIFICATION OF THE **ESCHERICHIA-COLI** PURINE REGULON REPRESSOR AND IDENTIFICATION OF COREPRESSORS.
AU ROLFES R J; ZALKIN H
CS DEP. BIOCHEM., PURDUE UNIV., WEST LAFAYETTE, INDIANA 47907.
SO J BACTERIOL, (1990) 172 (10), 5637-5642.
CODEN: JOBAAY. ISSN: 0021-9193.
FS BA; OLD
LA English

17 ANSWER 41 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
AB The Salmonella typhi galactose epimerase (**galE**) mutant strain Ty21a, a safe, effective, living, **attenuated** oral typhoid vaccine, was used as a recipient for a recombinant plasmid containing the gene for production of the nontoxic B subunit of the heat-labile enterotoxin of E. coli. The S. typhi derivative, strain SE12, produced heat-labile enterotoxin subunit B that was structurally and immunologically indistinguishable from heat-labile enterotoxin subunit B produced by strains of E. coli harboring the same plasmid. Tests in mice and guinea pigs showed that strain SE12 was safe when given orally and was capable of inducing a significant antitoxic antibody response when injected parenterally. It retained the galactose sensitivity of the parent strain, preserving its utility as a typhoid vaccine. This strain may prove to be a useful live oral bivalent vaccine strain for typhoid fever and cholera- and E. coli-related diarrheas.
AN 1985:269775 BIOSIS
DN BA79:49771
TI CONSTRUCTION OF A POTENTIAL LIVE ORAL BIVALENT VACCINE FOR TYPHOID FEVER AND CHOLERA-RELATED AND ESCHERICHIA-COLI RELATED DIARRHEAS.
AU CLEMENTS J D; EL-MORSHIDY S
CS DEPARTMENT MICROBIOLOGY AND IMMUNOLOGY, TULANE UNIVERSITY MEDICAL CENTER, NEW ORLEANS, LA. 70112.
SO INFECT IMMUN, (1984) 46 (2), 564-569.
CODEN: INFIBR. ISSN: 0019-9567.
FS BA; OLD
LA English

L17 ANSWER 36 OF 43 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8

AB We have recently described the construction of a **galE** derivative of Salmonella typhi Ty2 (Ty2H1) which had a 0.4-kilobase deletion in the **galE** gene and was sensitive to galactose-induced lysis when cultured with .gtoreq. 0.06 mM galactose (D. M. Hone, R. Morona, S. Attridge, and J. Hackett, J. Infect. Dis. 156:167-174, 1987). We now report the selection of a rifampin-resistant, via derivative of Ty2H1, EX462. Compared with the Ty2 parent strain, EX462 was serum sensitive and highly **attenuated** in the mouse mucin virulence assay. When four human volunteers ingested 7 .times. 108 viable EX462, two became ill and developed a typhoidlike disease with fever and bacteremia. Blood isolates from these individuals were indistinguishable from the vaccine strain by a variety of criteria. We concluded that, even in a via background, the **galE** mutation was not **attenuating** for S. typhi in humans.

AN 1988:288236 BIOSIS

DN BA86:16503

TI A GAL-1E VIA VI ANTIGEN-NEGATIVE MUTANT OF SALMONELLA-TYPHI TY2 RETAINS VIRULENCE IN HUMANS.

AU HONE D M; ATTRIDGE S R; FORREST B; MORONA R; DANIELS D; LABROOY J T; BARTHOLOMEUSZ R C A; SHEARMAN D J C; HACKETT J

CS DEP. MICROBIOL. IMMUNOL., UNIV. ADELAIDE,, ADELAIDE, S. AUSTRALIA 5001, AUST.

SO INFECT IMMUN, (1988) 56 (5), 1326-1333.
CODEN: INFIBR. ISSN: 0019-9567.

FS BA; OLD

LA English

L7 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AB Using purine auxotrophic strains of **Escherichia coli** with additional genetic lesions in the pathways of interconversion and salvage of purine compounds, we demonstrated the in vivo function of guanosine kinase and inosine kinase. Mutants with increased ability to utilize guanosine were isolated by plating cells on medium with guanosine as the sole purine source. These mutants had altered guanosine kinase activity and the mutations were mapped in the gene encoding guanosine kinase, gsk. Some of the mutants had acquired an additional genetic lesion in the purine de novo biosynthetic pathway, namely a purF, a purL or a purM mutation. A revised map location of the gsk gene is presented and the gene order established as proC-acrA-apt-adk-gsk-purE.

AN 1989:334384 BIOSIS

DN BA88:37384

TI ROLE OF GUANOSINE KINASE IN THE UTILIZATION OF GUANOSINE FOR NUCLEOTIDE SYNTHESIS IN **ESCHERICHIA-COLI**.

AU HOVE-JENSEN B; NYGAARD P

CS ENZYME DIV., UNIV. INST. BIOL. CHEM. B, SOLVGADE 83, DK-1307 COPENHAGEN K, DEN.

SO J GEN MICROBIOL, (1989) 135 (5), 1263-1274.
CODEN: JGMIAN. ISSN: 0022-1287.

FS BA; OLD

LA English

L32 ANSWER 28 OF 30 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB Previous studies have shown that high-temperature requirement A (**HtrA**) mutants of Brucella abortus are more sensitive to oxidative killing in vitro, are less able to survive in cultured murine macrophages and are **attenuated** in BALB/c mice. To measure the effect of an **HtrA** mutation on the virulence of B abortus in ruminants, pregnant goats in late gestation were exposed to infection by the conjunctival route with B abortus 2308 or an isogenic **htrA** mutant, PHE1. Infection with either 2308 or PHE1 resulted in abortion, but the serological responses to infection were consistent with 2308 but variable with PHE1. Strain 2308 was recovered post mortem both from aborted fetuses and infected dams, whereas PHE1 was recovered from neither. Nevertheless, short term studies revealed that PHE1 could be recovered from infected goats for up to two weeks after infection, suggesting that although the **HtrA** mutation may change the colonising ability of B abortus, the virulence of the mutant in pregnant goats is not reduced.

AN 96:205576 SCISEARCH

GA The Genuine Article (R) Number: TZ459

TI BEHAVIOR OF A HIGH-TEMPERATURE-REQUIREMENT-A (**HTRA**) DELETION MUTANT OF BRUCELLA-ABORTUS IN GOATS

AU ELZER P H (Reprint); HAGIUS S D; ROBERTSON G T; PHILLIPS R W; WALKER J V; FATEMI M B; ENRIGHT F M; ROOP R M

CS LOUISIANA STATE UNIV, DEPT VET SCI, CTR AGR, BATON ROUGE, LA, 70803 (Reprint); LOUISIANA STATE UNIV, MED CTR, DEPT MICROBIOL & IMMUNOL, SHREVEPORT, LA, 71130

CYA USA

SO RESEARCH IN VETERINARY SCIENCE, (JAN 1996) Vol. 60, No. 1, pp. 48-50. ISSN: 0034-5288.

DT Article; Journal

FS AGRI

LA ENGLISH

REC Reference Count: 22

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

32 ANSWER 29 OF 30 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB Bacterial stress response proteins of the high temperature requirement A (**HtrA**) family are serine proteases which appear to play an important role in scavenging oxidatively damaged proteins from the cell before they reach toxic levels. An isogenic **htrA** deletion mutant, designated RWP5, was constructed from virulent Brucella melitensis 16M via gene replacement to determine whether the B. melitensis **HtrA** protein functions as a stress response protein, and to evaluate the contribution of this protein to virulence. Unlike the parental strain, RWP5 would not form isolated colonies on solid media at 40 degrees C or grow on Schaedler agar without blood supplementation. RWP5 also grew poorly in broth culture in contrast to 16M. The B. melitensis **htrA** mutant was significantly more sensitive ($P < 0.001$) to killing by H2O2 and puromycin than the parental strain, and a significant reduction ($P < 0.001$) in the number of RWP5 recovered from the spleens and livers of experimentally infected BALB/c mice was observed at one week post infection compared to 16M. However, by 3 weeks post-infection and continuing thereafter through to 20 weeks post-infection, the levels of RWP5 and 16M recovered from the spleens and livers of experimentally infected mice were similar. In vitro and in vivo evaluation of RWP5 reisolates obtained from the spleens of mice at 4 and 16 weeks post-infection demonstrated that mouse passage did not significantly alter these characteristic in vitro and in vivo properties of RWP5. These results support a stress response function for the B. melitensis **HtrA** protein and suggest that this protein contributes to the pathogenesis of B. melitensis early in infection. The basis for the recovery of RWP5 at later timepoints in infected mice is presently unknown; however, the results presented here suggest that it is not caused by a stable genetic change resulting from mouse passage. (C) 1995 Academic Press Limited

AN 96:25279 SCISEARCH

GA The Genuine Article (R) Number: TK665

TI A BRUCELLA-MELITENSIS HIGH-TEMPERATURE-REQUIREMENT-A (**HTRA**) DELETION MUTANT DEMONSTRATES A STRESS-RESPONSE DEFECTIVE PHENOTYPE IN-VITRO AND TRANSIENT **ATTENUATION** IN THE BALB/C MOUSE MODEL

AU PHILLIPS R W; ELZER P H; ROOP R M (Reprint)

CS LOUISIANA STATE UNIV, MED CTR, DEPT MICROBIOL & IMMUNOL, 1501 KINGS HIGHWAY, POB 33932, SHREVEPORT, LA, 71130 (Reprint); LOUISIANA STATE UNIV, MED CTR, DEPT MICROBIOL & IMMUNOL, SHREVEPORT, LA, 71130

CYA USA

SO MICROBIAL PATHOGENESIS, (NOV 1995) Vol. 19, No. 5, pp. 277-284. ISSN: 0882-4010.

DT Article; Journal

FS LIFE

LA ENGLISH

ANSWER 40 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AB Mutations at several chromosomal locations affect expression of the major outer membrane porin proteins (**OmpF** and **OmpC**) of Escherichia coli K12. Those that map at 21 and 47 min define the structural genes for **OmpF** and **OmpC**, respectively. A 3rd locus, ompB, is defined by mutations that map at 74 min. The ompB locus contains 2 genes whose products regulate the relative amounts of **ompF** and **ompC** expression. One of these, **ompR**, encodes a positive regulatory protein that interacts at the **ompF** and **ompC** promoters. Mutations in **ompR** exhibit an **OmpF- OmpC-** or an **OmpF+ OmpC-** phenotype. The product of the 2nd gene, envZ, affects regulation of the porin proteins in an unknown manner. Previously isolated mutations in envZ exhibit an **OmpF- OmpC+** phenotype and also have pleiotropic effects on other exported proteins. In the presence of local anesthetics such as procaine, wild-type strains exhibit properties similar to these envZ **mutants**, i.e., **OmpF- OmpC+**. Using **OmpF**-lac fusion strains, this procaine effect was exploited to isolate 2 new classes of envZ mutations. One class exhibits an **OmpF+ OmpC-** phenotype. The other allows expression of both **OmpF** and **OmpC** but alters the relative amounts found under various growth conditions. Like previously isolated envZ mutations, these also affect regulation of other exported proteins, such as phage .lambda. receptor. These results permit a more detailed analysis of the omp regulon and they may shed light on 1 mechanism by which local anesthetics exert their effect.

AN 1984:177917 BIOSIS

DN BA77:10901

TI ISOLATION AND CHARACTERIZATION OF MUTATIONS ALTERING EXPRESSION OF THE MAJOR OUTER MEMBRANE PORIN PROTEINS USING THE LOCAL ANESTHETIC PROCAINE.

AU TAYLOR R K; HALL M N; SILHAVY T J

CS LAB. GENET. RECOMBINANT DNA, BASIC RES. PROGRAM-LBI, FREDERICK CANCER RES. FAC., FREDERICK, MD 21701, USA.

SO J MOL BIOL, (1983) 166 (3), 273-282.
CODEN: JMOBAK. ISSN: 0022-2836.

FS BA; OLD

LA English

L28 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS on STN

AB **Attenuated** immunogenic bacteria having an RpoS+ phenotype, in particular, Salmonella enterica serotype Typhi having an RpoS+ phenotype and methods therefor are disclosed. The Salmonella have in addn. to an RpoS+ phenotype, an inactivating mutation in one or more genes which render the microbe **attenuated**, and a recombinant gene capable of expressing a desired protein. The inactivated/mutated genes are selected from pab, **pur**, aro, asd, dap, nadA, pncB, balE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfe, poxA, galU, metL, metH, mviA, sodC recA, ssrA, ssrB , sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB and slyA gene. The Salmonella are **attenuated** and have high immunogenicity so that they can be used in vaccines and as delivery vehicles for genes and gene products. Also disclosed are methods for prepg. the vaccine delivery vehicles.

AN 2002:345842 CAPLUS

DN 136:354186

TI Recombinant vaccines comprising **attenuated** Salmonella having Rpos+ phenotype encoding a desired antigen

IN Curtiss, Roy, III; Nickerson, Cheryl A.

PA Washington University, USA

SO U.S., 50 pp., Cont.-in-part of U.S. 6,024,961.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6383496	B1	20020507	US 1999-314062	19990518
	US 6024961	A	20000215	US 1997-970789	19971114
	ES 2181306	T3	20030216	ES 1998-958581	19981113
	US 2003031683	A1	20030213	US 2002-138239	20020503
PRAI	US 1997-970789	A2	19971114		
	US 1999-314062	A1	19990518		

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AB Expression of the **ompC** and **ompF** genes coding for the major outer membrane proteins, **OmpC** and **OmpF**, respectively, is known to be controlled by at least two regulatory genes, **ompR** and envZ, which together comprise a single ompB operon. We constructed chromosomal mutants with either **ompR**-envZ deletion or envZ deletion. Characterization of these deletion or strains showed that the **OmpR** protein is necessary for transcription of the **ompC** and **ompF** genes, and the EnvZ protein is essential for normal regulation of the **ompC** and **ompF** expression, which is affected by the medium osmolarity. We also constructed several plasmids carrying different portions of the ompB operon. Characterization of these plasmids allowed us to identify the **OmpR** protein with an apparent molecular weight of 29 kilodaltons (kDa) and the EnvZ protein with an apparent molecular weight of 50 kDa. The initiation codon for EnvZ translation appeared to overlap with the termination codon for **OmpR** translation. It was also found that a truncated EnvZ polypeptide (44 kDa) which lacks the N-terminal 55 amino acid residues can complement the envZ deletion mutant. Based on these results, the structure and function of the ompB operon are discussed in relation to the regulation of **ompC** and **ompF** expression.
AN 1987:294701 BIOSIS
DN BA84:24733
TI ISOLATION AND CHARACTERIZATION OF **DELETION MUTANTS** OF OMP-R AND ENV-Z REGULATORY GENES FOR EXPRESSION OF THE OUTER MEMBRANE PROTEINS **OMPC** AND **OMPF** IN ESCHERICHIA-COLI.
AU MIZUNO T; MIZUSHIMA S
CS LAB. MICROBIOL., SCH. AGRIC., NAGOYA UNIV., CHIKUSA-KU, NAGOYA 464.
SO J BIOCHEM (TOKYO), (1987) 101 (2), 387-396.
CODEN: JOBIAO. ISSN: 0021-924X.
FS BA; OLD
LA English

QR501.J6 QP581.J6

L10 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AB In Escherichia coli the histidine kinase sensor protein, EnvZ, undergoes autophosphorylation and subsequently phosphorylates the regulatory protein, **OmpR**. Modulation of the levels of **OmpR**-phosphate controls the differential expression of **ompF** and **ompC**. While the phosphotransfer reaction between EnvZ and **OmpR** has been extensively studied, the domains involved in the sensing function of EnvZ are not well understood. We have used a comparative approach to study the sensing function of EnvZ. During our search of numerous bacteria we found that the symbiotic/pathogenic bacterium Xenorhabdus nematophilus contained the operon encoding both **ompR** and envZ. Nucleotide sequence analysis revealed that EnvZ of X. nematophilus (EnvZ(X.n.)) is composed of 342 amino acid residues, which is 108 residues shorter than EnvZ of E. coli (EnvZ(E.c.)). Amino acid sequence comparison showed that the cytoplasmic domains of the EnvZ molecules shared 57% sequence identity. In contrast, the large hydrophilic periplasmic domain of EnvZ(E.c.) was absent in EnvZ(X.n.), and was replaced by a shorter hydrophobic region. Although the periplasmic domains had diverged extensively, envZ(X.n.) was able to complement a Delta envZ strain of E. coli. **OmpF** and **OmpC** were differentially produced in response to changes in medium osmolarity in this strain. Further genetic analysis established that heterologous phosphorylation between EnvZ(X.n.) and **OmpR** of E. coli(**OmpR**(E.c.)) accounted for the complementation of the Delta envZ strain. In addition we show that the **OmpR** molecules of X. nematophilus and E. coil share 78% amino acid sequence identity. These results indicate that the EnvZ protein of X. nematophilus was able to sense changes in the osmolarity of the growth environment and properly regulate the levels of **OmpR**-phosphate in E. coli.
AN 95:669038 SCISEARCH
GA The Genuine Article (R) Number: RW445

L17 ANSWER 38 OF 43 LIFESCI COPYRIGHT 2003 CSA on STN

AB Live **attenuated** strains of salmonellae are showing promise as live oral vaccines against human typhoid fever and other Salmonella infections of man and animals. **Attenuation** can be achieved by introducing genetically defined, non-reverting mutations into specific genes on the Salmonella chromosome. Mutations in the **galE** or aroA genes of Salmonella inhibit the ability of the bacteria to grow in vivo, and strains carrying such lesions are effective vaccines against salmonellosis. Genetic determinants encoding for the expression of potentially protective antigens from heterologous, non-Salmonella pathogens can be readily introduced into these **attenuated** Salmonella strains. Expression of the heterologous antigen does not affect the ability of the Salmonella host to be used as a Salmonella vaccine. Mice infected orally with a Salmonella typhimurium aroA vaccine expressing the Escherichia coli heat-labile toxin B subunit developed both a secretory and serum antibody response to this antigen. These serum antibodies were able to neutralise the activity of E. coli heat-labile toxin in tissue culture assays.

AN 87:12295 LIFESCI

TI Live oral Salmonella vaccines: Potential use of **attenuated** strains as carriers of heterologous antigens to the immune system.

AU Dougan, G.; Hormaeche, C.E.; Maskell, D.J.

CS Wellcome Res. Lab., Langley Court, Beckenham, Kent BR3 3BS, UK

SO PARASITE IMMUNOL., (1987) vol. 9, no. 2, pp. 151-160.

DT Journal

FS J; F; W; A

LA English

SL English

L20 ANSWER 46 OF 48 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 90:425536 SCISEARCH
GA The Genuine Article (R) Number: DR471
TI **SURA**, AN **ESCHERICHIA-COLI** GENE ESSENTIAL FOR SURVIVAL IN STATIONARY PHASE
AU TORMO A; ALMIRON M; KOLTER R (Reprint)
CS HARVARD UNIV, SCH MED, DEPT MICROBIOL & MOLEC GENET, 200 LONGWOOD AVE, BOSTON, MA, 02115
CYA USA
SO JOURNAL OF BACTERIOLOGY, (1990) Vol. 172, No. 8, pp. 4339-4347.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 43

21 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 8

AB In E. coli **cya** mutants, deficient in adenylate cyclase (EC 4.6.1.1), basal cellular rates of glycogen synthesis were lower and the relative increases produced by exogenous cAMP during growth on glucose were greater than in their resp. parent strains. These observations provide strong evidence that endogenous cAMP is one of the key regulators of glycogen synthesis in growing E. coli. In crp mutants, deficient in cAMP receptor protein (CRP), the basal cellular rates of glycogen synthesis were much lower than in their resp. parent strains. Stimulation of glycogen synthesis by exogenous cAMP was markedly **attenuated** in the 3 crp mutants. Thus, stimulation of glycogen synthesis by either endogenous or exogenous cAMP appears to require CRP. Functional CRP appeared to be required for all 3 responses obsd. after cAMP addn.: an abrupt step-up in the cellular rate of glycogen synthesis, a continuing exponential increase in rate, and a stimulation of the rate during a subsequent N starvation. To account for these responses, a math. model was derived in which the cAMP-CRP complex regulates the differential rate of synthesis of an enzyme metabolizing an effector of the rate-limiting enzyme of glycogen synthesis.

AN 1983:157663 CAPLUS

DN 98:157663

TI Regulation of bacterial glycogen synthesis. Stimulation of glycogen synthesis by endogenous and exogenous cyclic adenosine 3':5'-monophosphate in **Escherichia** coli and the requirement for a functional CRP gene

AU Leckie, Mary P.; Ng, Ronald H.; Porter, Sharon E.; Compton, David R.; Dietzler, David N.

CS Sch. Med., Washington Univ., St. Louis, MO, 63110, USA

SO Journal of Biological Chemistry (1983), 258(6), 3813-24
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

1 ANSWER 26 OF 28 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB In recent years there has been a resurgence of research to develop new and improved **attenuated** strains of Salmonella typhi to function as live oral vaccines against typhoid fever and to serve as "carrier" vaccines to express foreign antigens of other pathogens and deliver them to the immune system. Strain Ty21a has served as a prototype in clinical and field trials to identify the optimal formulations and dosage schedules for live vaccines and to quantitate the duration of protection that can be achieved. Clinical trials with three new **attenuated** S. typhi candidate vaccines, a Vi+ variant of Ty21a, an aroC,aroD double mutant recombinant strain and a **cya**,crp double mutant, are underway or will be initiated shortly.

AN 91:17776 SCISEARCH

GA The Genuine Article (R) Number: EQ001

TI CLINICAL AND FIELD TRIALS WITH **ATTENUATED** SALMONELLA-TYPHI AS LIVE ORAL VACCINES AND AS CARRIER VACCINES

AU LEVINE M M (Reprint); HONE D; TACKET C; FERRECCIO C; CRYZ S

CS UNIV MARYLAND, SCH MED, CTR VACCINE DEV, DEPT MED, DIV GEOG MED, 10 S PINE ST, BALTIMORE, MD, 21201 (Reprint); UNIV MARYLAND, CTR MED BIOTECHNOL, INST BIOTECHNOL, BALTIMORE, MD, 21201; MINIST HLTH SANTIAGO, TYPHOID FEVER & ENTER INFECT CONTROL PROGRAM, SANTIAGO, CHILE; SWISS SERUM & VACCINE INST, BERN, SWITZERLAND

CYA USA; CHILE; SWITZERLAND

SO RESEARCH IN MICROBIOLOGY, (1990) Vol. 141, No. 7-8, pp. 807-816.

DT Article; Journal

FS LIFE

LA ENGLISH

REC Reference Count: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

21 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

AB **Attenuated** Salmonella for use as live vaccines against Salmonella and other Gram-neg. bacteria are prepd. The organisms are incapable of manufg. the lipopolysaccharide involved in pathogenesis because of mutation in several genes involved in the synthesis of, or regulation of synthesis of, the lipopolysaccharide. Other genes involved in the regulation of pathogenesis-related genes are also inactivated. A S. typhimurium with the crp and **cya** genes deleted was prepd. by transposon mutagenesis with Tn10. S. typhimurium carrying both deletions had an LD50 of >109 colony-forming units (CFU) in Leghorn chicks, vs. 2 .times. 104 - 2 .times. 105 for wild-types. Similar deletions of the phoP, fur, pmi, and galE genes were constructed. Some of the constructs prepd. were found to confer cross-resistance to S. enteriditis and pathogenic **Escherichia** coli.

AN 1991:469825 CAPLUS

DN 115:69825

TI Cross-protective Salmonella vaccines using multiply mutant S. typhimurium

IN Curtiss, Roy, III; Munson, Maryann

PA Washington University, USA

SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9106317	A1	19910516	WO 1990-US6503	19901102
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2072633	AA	19910504	CA 1990-2072633	19901102
	AU 9067371	A1	19910531	AU 1990-67371	19901102
	EP 500699	A1	19920902	EP 1990-917076	19901102
	EP 500699	B1	19980610		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
	JP 05504331	T2	19930708	JP 1990-515888	19901102
	AT 167061	E	19980615	AT 1990-917076	19901102
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L32 ANSWER 26 OF 30 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

AB We compared the abilities of different Salmonella enterica var, Typhimurium (S, typhimurium) strains harboring mutations in the genes aroA, aroAD, purA, ompR, **htrA**, and cya crp to present the heterologous antigen, C fragment of tetanus toxin, to the mouse immune system, Plasmid pTETtac4, encoding C fragment, was transferred into the various S, typhimurium mutants, and the levels of antigen expression were found to he equivalent, After primary oral immunization of BALB/c mice, all **attenuated** strains were capable of penetrating the gut epithelium and colonizing the Peyer's patches and spleens of mice, Of all strains compared, the Delta purA mutant colonized and persisted in the Peyer's patches at the lowest level, whereas the Delta **htrA** mutant colonized and persisted in the spleen at the lowest level, The level of specific antibody elicited by the different strains against either S, typhimurium lipopolysaccharide or tetanus toroid was strain dependent and did not directly correlate to the mutants' ability to colonize the spleen, The level of immunoglobulin G1 (IgG1) and IgG2a antibody specific for tetanus toroid was determined in mice immunized with four S, typhimurium mutants, The level of antigen-specific IgG1 and IgG2a was significantly lower in animals immunized with S, typhimurium Delta purA. Antigen-specific T-cell proliferation assays indicated a degree of variability in the capacity of some strains to elicit T cells to the heterologous antigen. Cytokine profiles (gamma interferon and interleukin-5) revealed that the four S, typhimurium mutants tested induced a Th1-type immune response, Mice were challenged with a lethal dose of tetanus toxin 96 days after oral immunization, With the exception of the S, typhimurium Delta purA mutant, all strains elicited a protective immune response. These data indicate that the level of total Ig specific for the carried antigen, C fragment, does not correlate with the relative invasiveness of the vector, but it is determined by the carrier mutation and the background of the S, typhimurium strain.

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TI Comparison of the abilities of different **attenuated** Salmonella typhimurium strains to elicit humoral immune responses against a heterologous antigen

AU Dunstan S J (Reprint); Simmons C P; Strugnell R A

CS UNIV MELBOURNE, DEPT IMMUNOL & MICROBIOL, PARKVILLE, VIC 3052, AUSTRALIA (Reprint); UNIV MELBOURNE, COOPERAT RES CTR VACCINE TECHNOL, PARKVILLE, VIC 3052, AUSTRALIA

CYA AUSTRALIA

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DUPLICATE 4

AB In **Escherichia** coli, extracytoplasmic stress is partially controlled by the alternative sigma factor, RpoE (sigmaE). In response to environmental stress or alteration in the protein content of the cell envelope, sigmaE upregulates the expression of a number of genes, including **htrA**. It has been shown that **htrA** is required for intramacrophage survival and virulence in Salmonella typhimurium. To investigate whether sigmaE-regulated genes other than **htrA** are involved in salmonella virulence, we inactivated the rpoE gene of S. typhimurium SL1344 by allelic exchange and compared the phenotype of the mutant (GVB311) in vitro and in vivo with its parent and an isogenic **htrA** mutant (BRD915). Unlike E. coli, sigmaE is not required for the growth and survival of S. typhimurium at high temperatures. However, GVB311 did display a defect in its ability to utilize carbon sources other than glucose. GVB311 was more sensitive to hydrogen peroxide, superoxide, and antimicrobial peptides than SL1344 and BRD915. Although able to invade both macrophage and epithelial cell lines normally, the rpoE mutant was defective in its ability to survive and proliferate in both cell lines. The effect of the rpoE mutation on the intracellular behavior of S. typhimurium was greater than that of the **htrA** mutation. Both GVB311 and BRD915 were highly **attenuated** in mice. Neither strain was able to kill mice via the oral route, and the 50% lethal dose (LD50) for both strains via the intravenous (i.v.) route was very high. The i.v. LD50s for SL1344, BRD915, and GVB311 were <10, 5.5 X 105, and 1.24 X 107 CFU, respectively. Growth in murine tissues after oral and i.v. inoculation was impaired for both the **htrA** and rpoE mutant, with the latter mutant being more severely affected. Neither mutant was able to translocate successfully from the Peyer's patches to other organs after oral infection or to proliferate in the liver and spleen after i.v. inoculation. However, the **htrA** mutant efficiently colonized the livers and spleens of mice infected i.v., but the rpoE mutant did not. Previous studies have shown that salmonella **htrA** mutants are excellent live vaccines. In contrast, oral immunization of mice with GVB311 was unable to protect any of the mice from oral challenge with SL1344. Furthermore, i.v. immunization with a large dose (apprx 106 CFU) of GVB311 protected less than half of the orally challenged mice. Thus, our results indicate that genes in the sigmaE regulon other than **htrA** play a critical role in the virulence and immunogenicity of S. typhimurium.

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TI The alternative sigma factor, sigmaE, is critically important for the virulence of Salmonella typhimurium.

AU Humphreys, Sue; Stevenson, Andrew; Bacon, Andrew; Weinhardt, A. Barbara; Roberts, Mark (1)

CS (1) Department of Veterinary Pathology, Glasgow University Veterinary School, Bearsden Rd., Glasgow, G61 1QH UK

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